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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte DONALD L. MORTON, RISHAB K. GUPTA, and DAVID M. EUHUS

Appeal 2007-4481
Application 07/431,533
Technology Center 1600

Decided: July 30, 2008

Before, DEMETRA J. MILLS, ERIC GRIMES, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

The following claims are representative.

62. An antigen composition comprising a substantially purified tumor antigen, wherein the tumor antigen is identified as comprising Urinary Tumor Associated Antigen (UTAA) subunit which, after reduction by ß-mercaptoethanol and separation by SDS-polyacrylamide gel electrophoresis,

exhibits a molecular weight of about 90 to 100 kD, and wherein said subunit contains glycosidase-sensitive carbohydrates, is heat stable at 100°C, and has an isoelectric point of about 6.1.

69. The composition of claim 62, wherein said UTAA is about 95% free of immunoglobulin.

Cited References

Goldenberg US 4,348,376 Sep. 7, 1982

Siv Ljungquist, "A New Endonuclease from *Esherichia coli* Acting at Apurinic Sites in DNA," 252 (9) *The Journal of Biological Chemistry* 2808-2814 (May 1977).

Neal S. Rote et al., "Tumor-Associated Antigens Detected by Autologous Sera in Urine of Patients with Solid Neoplasms," 29 *Journal of Surgical Research*, 18-22 (1980).

Gel Filtration, Theory and practice, (*Pharmacia Fine Chemicals*, 1980), 4, 14, 26-27 (hereafter "Gel Filtration").

Ion Exchange Chromatography, Principles and methods (*Pharmacia Fine Chemicals*), 3-7, 43-47 (1980) (hereafter "Ion Exchange Chromatography").

Sanford J. Finck et al., "Excretion of Tumor-Associated Antigens(s) in the Urine of Patients With Colon Carcinoma," 21 *Journal of Surgical Oncology*, 81-86 (1982).

Hans-Dieter Hofman et al., "Characterization and Partial Purification of a Novel Neuronotrophic Factor from Bovine Seminal Vesicle", 48 (5) *Journal of Neurochemistry*, 1425-1433 (1987).

D. Euhus et al., "Demonstration And Isolation Of A Glycoprotein Tumor Associated Antigen From Sera Of Melanoma Patients," 7 (abstract no. 169) *Proceedings of American Society of Clinical Oncology*, 44 (March 1998).

Andrew R. Exley et al., "Optimal Collection Of Blood Samples For The Measurement Of Tumor Necrosis Factor α," 2 (5) *Cytokine*, 353-356 (Sept. 1990).

Grounds of Rejection

1. Claims 19[1], 62, 65 and 73-79 stand rejected under 35 U.S.C. 112, second paragraph.

2. Claims 19, 62-66, 69-70, and 72-79 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Euhus, in view of Exley, Rote, or Finck, Gel Filtration, Ion Exchange Chromatography, Ljungquist, Goldenberg, further in view of Hofmann.

DISCUSSION

Background

This invention relates generally to "tumor-associated antigens, specifically to an antigen found in the urine of cancer patients which can be used for immunodiagnosis, immunoprognosis, and therapy of human cancer." (Spec. 1.)

1. Claims 62, 65 and 73-79 stand rejected under 35 U.S.C. 112, second paragraph for indefiniteness. We select claim 62 as representative of this rejection as individual claims are not argued separately.

The Examiner contends that claims 62, 65 and 73-79 are indefinite because claims 62 and 73 recite the language "substantially" purified, "which does not set forth the metes and bounds of the patent protection

[1] Appellants note that claim 19 was cancelled (*see* Rep. Br. 3).

desired. The term 'substantially' in the claims is a relative term which renders the claims indefinite." (Ans. 6.) "The term 'substantially' is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention." (Ans. 6.)

Appellants contend that there are a number of distinct indicators of what purity can be achieved in these systems set forth in the Specification, including "(a) UTAA protein compositions that are purified about 100-fold and 105-fold over UTAA found in urine, (b) UTAA present as at least about 0.6% of total protein in the composition; and (c) UTAA at about 95% and 99.5% free of immunoglobulin. The Examiner's only response is to state that because the degree of purity is not included in the claims, they are indefinite. This is not an argument nor is it reasoning - it is a conclusion." (Reply Br. 5.)

"The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification." *Miles Laboratories, Inc. v. Shandon, Inc.*, 997 F.2d 870, 875 (Fed. Cir. 1993).

In our view the Specification citations provided herein by Appellants, as well as the ordinary meaning of the term "substantially purify", provide one of ordinary skill in the art with an understanding of the degree of purity encompassed by the claims. Simply because the term "substantially" is broad, does not make the term indefinite. "[B]readth is not to be equated with indefiniteness." *In re Miller*, 441 F.2d 689, 693 (CCPA 1971). We find

Appellants have the better argument and the rejection for indefiniteness is reversed.

2. Claims 62-66, 69-70, and 72-79 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Euhus, in view of Exley, Rote, or Finck, Gel Filtration, Ion Exchange Chromatography, Ljungquist, Goldenberg, further in view of Hofmann.

When determining whether a claim would have been obvious, an Examiner must make "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995). Thus, "obviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)). "[W]hen the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990).

The Examiner acknowledges that:

> Euhus et al. do not teach that UTAA contains glycosidase-sensitive carbohydrates, is heat stable at 100°C and has an isoelectric point of about 6.1. Euhus et al. do not teach that UTAA is purified at least about 100-fold, or 105-fold over UTAA found in urine.

(Ans. 8.)

However, the Examiner argues that:

> Euhus et al teach isolation of UTAA, which has the same following properties as the claimed UTAA: 1) similar to the claimed UTAA, UTAA taught by Euhus et al is from sera or urine of melanoma patients, and 2) UTAA taught by Euhus et al has a molecular weight at about 111 kD under SDS-PAGE, which is not significantly different from the molecular weight of about 90 to 100 kD under SDS-PAGE of the claimed UTAA. Further, similar to the disclosure of the specification (see Example 1, isolation of UTAA from urine, in [S]pecification, pages 22-23, and Example XI, isolation of UTAA from serum, in specification, pages 33-34), Euhus [] teach that UTAA is free of IgG and IgM, and could be isolated by gel filtration, and DEAE anion exchange chromatography, and detected using autologous or allogenic antibody in ELISA. Although Euhus [] do not teach in details how to perform ELISA, gel filtration and DEAE anion exchange chromatography, such techniques are routine in the art, and are provided by the secondary references.

(Ans. 17-18.)

In addition, both the Specification and Euhus teach that UTAA resolves as four bands by SDS-polyacrylamide gel electrophoresis. (Spec. 16, Euhus, Abstract.) Further, the two bands whose specific molecular weight is given by Euhus, at 142 kD and 111 kD are identified as corresponding "to those present in U-TAA from urine" (Euhus, Abstract) and are substantially similar in size to the two bands disclosed in the Specification (Spec. 16).

The Examiner argues that under the principles of *In re Best*, that "[t]he office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the

claimed product." (Answer 13.) Thus, the burden is properly shifted to the Appellants to provide evidence that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best,* 562 F.2d 1252 (CCPA 1977), and *Ex parte Gray,* 10 USPQ2d 1922 (BPAI 1989).

Having established that the claimed product and the Euhus UTAA product are the same or substantially the same for the reasons articulated in the Answer, the Examiner concludes

> it would have been *prima facia* obvious to a person of ordinary skill in the art at the time the invention was made to purify UTAA from urine or serum samples of melanoma patients, using the purification methods taught by Euhus et al, wherein the details of said methods are taught by Pharmacia, Ljungquist, and Hofmann et al. It would have been obvious to use the ELISA detection methods taught by Euhus et al, wherein the details of said methods are taught by Exley et al, and the antibodies for detection are from autologous or alleogenic sera of melanoma patients, as taught by Euhus et al, Rote et al, and Finck et al. …The isolated UTAA, as taught by Euhus et al, would be the same as the claimed UTAA, which is isolated from urine and sera of melanoma patients, because urine and serum samples of melanoma patients could be used for UTAA isolation, wherein UTAA is originally found in urine of melanoma patients, and wherein the molecular weight (111 kD) of a subunit of UTAA taught by Euhus et al. is not significantly different from that of the claimed UTAA, having a molecular weight from about 90 kD to about 100 kD. Furthermore, the urine and serum samples of melanoma patients, that one of ordinary skill in the art could use for UTAA purification, would be the same as those used by applicant, because there is no specific teaching in the claims and the [S]pecification concerning any specific properties of urine and serum samples from melanoma patients which are used for UTAA purification.

(Ans. 11-12.)

Appellants contend that the Euhus reference is not enabling for the isolation of UTAA. (Br. 10.) Appellants argue, "the teachings of Euhus are not sufficient to permit one to reproducibly make and use the invention." (Br. 10.)

In particular, Appellants acknowledge that the Examiner provides an extensive discussion of how one could use autologous sera to find such antigens once they had been fractionated. (Reply Br. 7.) Appellants argue, however, that

> [a]ssuming one could isolate ***some*** fraction containing UTAA, how would one know that they had purified the correct antigen ***or*** the correct antibodies, much less identify a patient that even contained these substances? The answer, of course, is that they could not know since the prior art fails to teach which fraction contained UTAA, or how one could identify UTAA from any other protein using any readily obtainable, well-characterized antibodies.

(Reply Br. 7.)

Appellants argue that the cited prior art is nothing more than an acknowledgement that something called UTAA exists, along with a collection of general techniques that might purify UTAA, without any indication of how to confirm this or to identify which fraction actually contains UTAA. Thus, Appellants argue there is a major difference in the enabling quality of the present Specification and the Euhus reference. (Reply Br. 8.)

"Normally, when an Examiner compares the subject matter of a claim pending in an application with an individual prior art reference, the

Examiner will determine whether a difference exists between the two. If no difference exists, the reference would be considered an anticipation under 35 U.S.C. § 102. If a difference exists, the reference becomes at best evidence under 35 U.S.C. § 103. However, *In re Best* is directed to a particular set of circumstances where Examiners in the USPTO cannot readily determine whether a difference exists between the subject matter of a given claim and a particular prior art document. Typically these circumstances arise in the context of a claim directed to a compound or composition where the claim describes a property or a function of the compound or composition which the prior art reference does not address. . . . In order to invoke the principles of *In re Best*, the Examiner must first make factual findings which support the conclusion that the claimed and prior art products prima facie are 'identical or substantially identical.'" *Ex parte Imori*, 2002 WL 1801301 (BPAI 2002).

We find that the Examiner has presented sufficient evidence as to why it is believed that the UTAA product of Euhus and the claimed product are the same or substantially the same to shift the burden to Appellants to prove that the products are different.

Appellants have argued that Euhus is non-enabling as to how to isolate the UTAA product. (Br. 10.) We are not persuaded by this argument. "[T]he proper test of a description in a publication as a bar to a patent as the clause is used in section 102(b) requires a determination of whether one skilled in the art to which the invention pertains could take the description of the invention in the printed publication and combine it with his own knowledge of the particular art and from this combination *be put in*

possession of the invention on which a patent is sought. Unless this condition prevails, the description in the printed publication is inadequate as a statutory bar to patentability under section 102(b)." *In re Sasse,* 629 F.2d 675, 681 (C.C.P.A. 1980). "[W]hen the PTO cited a disclosure which expressly anticipated the present invention, … the burden was shifted to the applicant. He had to rebut the presumption of the operability … by a preponderance of the evidence." *Id.*; *In re Jacobs*, 318 F.2d 743 (CCPA 1963).

In *In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985), the Examiner had made a rejection under 35 U.S.C. 102(b) over a publication, which disclosed the claimed compound, in combination with two patents teaching a general process of making the particular class of compounds. The Applicant submitted an affidavit stating that the authors of the publication had not actually synthesized the compound. The court held that the fact that the publication's author did not synthesize the disclosed compound was immaterial to the question of reference operability. The patents were evidence that synthesis methods were well known.[2] We find this case to be

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[2] Compare, *Ex parte Goldgaber*, 41 USPQ2d 1172 (BPAI 1995) (Subject matter of application claim for cDNA encoding brain beta-amyloid polypeptide associated with Alzheimer's disease would have been prima facie obvious based on combined disclosures of two references on which examiner based rejection, since person of ordinary skill in art would have been motivated to isolate claimed cDNA, since primary reference puts person of ordinary skill in possession of two sets of fully degenerate oligonucleotide probes suitable for isolating that cDNA, since person of ordinary skill in art would have been familiar with techniques for constructing and screening cDNA libraries described in second reference,

tangentially relevant to the facts before us. We find that Euhus teaches that after fractionation, gel filtration chromatography, and DEAE anion exchange chromatography UTAA having a specific molecular weight was recovered from sera of a melanoma patient free of IgG and IgM and separated into four bands in SDS-PAGE. Because the pending claims do not specify a specific level of purity of UTAA and because the procedures delineated in Euhus would provide for both isolation and purification to some extent of UTAA, we agree with the Examiner that the prior art disclosure of UTAA and disclosure of methods of isolation and properties of UTAA taken with references disclosing known methods of isolation of proteins is enabling for obtaining UTAA without undue experimentation.

In further support of patentability, Appellants put forth a Declaration of Dr. Reisfeld filed Dec. 18, 1996 and a Declaration of Dr. Shively. The Declarations purport to evidence that the primary reference, Euhus, is non-enabling for isolation of UTAA. We are not persuaded by these Declarations.

In particular, Dr. Reisfeld alleges that Euhus fails to disclose the amino acid sequence of UTAA or a meaningful description of the molecule. (Reisfeld Declaration ¶ 2.)[3] Dr. Reisfeld argues that one of ordinary skill in the art would not know if they had isolated the UTAA molecule of Euhus.

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and since it would have been well within skill of art to sequence isolated DNA rapidly and routinely at time invention was made.)

[3] Two Declarations of Dr. Reisfeld are of record, one filed April 26, 1996 and one filed December 18, 1996. The Declaration filed April 26 is essentially cumulative with the Declaration filed December 18. Reference is made herein to the Declaration filed December 18, 1996.

The Shively Declaration alleges that one of ordinary skill in the art would understand that Euhus does not contain sufficient information to enable purification of UTAA. (Shively Declaration ¶ 2.)

"The Board has broad discretion as to the weight to give to Declarations offered in the course of prosecution. *See Velander v. Garner*, 348 F.3d 1359, 1371 (Fed. Cir. 2003) ('[A]ccord[ing] little weight to broad conclusory statements [in expert testimony before the Board] that it determined were unsupported by corroborating references [was] within the discretion of the trier of fact to give each item of evidence such weight as it feels appropriate.')" (alterations in original). *In re American Academy of Science Tech Center*, 367 F.3d 1359, 1368 (Fed. Cir. 2004). In the present case, declarants Reisfeld and Shively's statements are merely conclusory in nature and are unaccompanied by supporting facts. The Declarations address the Euhus abstract in isolation and fail to take account of the knowledge of those skilled in the art as evidenced by the secondary references cited by the Examiner, and fail to allow for a reasonable amount of experimentation as is customary to those of ordinary skill in the art, to isolate UTAA. That is, there is no accompanying data or facts as to why the procedures outlined in Euhus, taken with purification techniques well known in the art, would fail to isolate UTAA. Affidavits and declarations fail in their purpose when they recite conclusions with few facts to buttress the conclusions. See *In re Brandstadter*, 484 F.2d 1395, 1406 (CCPA 1973) and *In re Thompson*, 545 F.2d 1290, 1295 (CCPA 1976) and *In re Beattie*, 974 F.2d 1309, 1313 (Fed. Cir. 1992).

In view of the above, we are not convinced that one of ordinary skill in the art would not have been able to purify or obtain the UTAA by the methods described in Euhus and known to those of ordinary skill in the art.

Claims 63, 64, 66, 69 and 70

Appellants argue claims 63, 64, 66, 69 and 70 are separately patentable. (Br. 18.) We select claim 69 as representative of this grouping of claims since Appellants have not separately argued the claims. 37 C.F.R. 41.37(c)(1)(vii).

Appellants argue that Euhus does not indicate that UTAA is free of other immunoglobulin species other than IgG and IgM. (Br. 18.)

The Examiner acknowledges that:

> Although Euhus et al teach that the purified antigen is free of IgM and IgG, and could be separated into two fractions of 142 kD and 111 kD under SDS-PAGE; Euhus et al do not teach that the purified antigen is 95 % or 99.5 % free of immunoglobulin.

(Ans. 17.)

However, the Examiner relies on:

> Hofman [] [as] teach[ing] a combination of gel filtration and SDS-PAGE gel slice elution for purifying a protein, wherein the SDS-PAGE step would further purify the protein from another protein, which is usually associated with the purified protein.

(Ans. 17.)

Therefore the Examiner concludes that:

> [O]ne of ordinary skill in the art would have expected that UTAA isolated by the combination methods taught by Euhus et al and Hofman et al would be at least 95 % or 99.5 % free of immunoglobulin, because of the following reasons: The gel slice containing UTAA at a molecular weight of 111 kD would not contain immunoglobulin, which is well known in the art to have a molecular weight of about 150 kD. In addition, the [S]pecification does not disclose any purification of UTAA from Ig's other than IgG and IgM, and the claims do not specify that UTAA is 95 % or 99.5 % free of Ig's other than IgG and IgM.

(Ans. 17.)

The Examiner further argues that:

> One of ordinary skill in the art would have expected that after gel filtration, as taught by Euhus et al, a urine sample from a melanoma patient would yield the same UTAA with the same degree of purity as the claimed UTAA since the urine samples taught by Euhus et al are the same as the claimed urine samples and the protocol of purification is the same, i.e., gel filtration.

(Ans. 26.)

We find no error in the Examiner's prima facie case of obviousness of claim 69. As discussed above, we find that the burden has shifted to Appellants to show that the UTAA claimed is not the same as that of Euhus. That burden has not been met by Appellants and the rejection is affirmed.

SUMMARY

The obviousness rejection is affirmed. The indefiniteness rejection is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

Ssc:

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